66. An animal feed derived at least in part from the genetically modified cruciferous plant or descendant thereof of claim 49.

REMARKS

Claims 11-14, 17, 19-26, directed to non-elected subject matter, have been cancelled without prejudice to Applicants' entitlement to continue the prosecution of these claims by way of a divisional application.

New claims 34-48 correspond generally with claims 1-10, and 15-16 of record, and find support therein. Claims 34-48 are directed to a method for altering a nutritional profile of a plant. Support for this amendment is found in the original specification at, e.g., page 18, line 16 through page 19, line 21, wherein anti-nutritional compounds are discussed.

New claims 49-65 correspond generally with original claims 16, 18, and 27-32 of record, and find support therein. The original claims were presented in a product-by-process form, making reference to original method claims 1-16. The instant claims are recast in the form of claims drawn to compositions of matter, without process limitations, and incorporate subject matter from claims 1-16 of record, and find support therein.

Claim 66 corresponds to and finds support in original claims 2, 16, and 33.

Composition of matter claims 49-66 are, like new method claims 34-48, drawn to the anti-nutritional aspects of the invention, and in this aspect find support in the specification and claims of record on the same basis.

Concerning 35 USC § 102

Claims 1, 2, 5-9, 16, 18, and 27-30 of record stand rejected under 35 USC § 102(b) as being anticipated by Murata (EP 0 818 138 A1).

Applicants respectfully submit that the presently amended claims patentably distinguish from Murata.

Murata teaches transformation of *Arabidopsis thaliana* and rice with a gene encoding the enzyme choline oxidase, for the purpose of producing salt- or osmo-tolerant plants. Such plants would be useful for greening desert or salt-accumulated areas. Murata teaches that expression of the choline oxidase gene in transformed plants results in the oxidation of choline to glycinebetaine, an osmo-protective agent.

Murata is concerned solely with the production of salt-tolerant or osmotolerant plants, and does not concern methods for altering a nutritional profile of a plant.

In contrast, the aspect of the instant invention presently under examination concerns methods for altering the nutritional profile of a plant, particularly by modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of the plant. Of particular interest are cruciferous plants, wherein the secondary metabolic pathway that is affected is the phenylpropanoid pathway. As discussed in the instant specification at, for instance, page 18, line 16 through page 19, line 21, cruciferous plants produce, by way of the phenylpropanoid pathway, a variety of phenolic compounds, which are anti-nutritional factors when present in animal feed. Because in many cruciferous plants, the seed is a particularly important source of feed products, alteration of the content of various phenolic compounds in the seed is an important commercial objective.

Murata, who was concerned only with salt-tolerance, and who did not contemplate the problem of anti-nutritional compounds in plants useful as animal feeds, did not genetically modify plants to alter their nutritional profile.

Indeed, *Arabidopsis thaliana* which, although a crucifer, is essentially a weed that is useful as a research tool, but that is not useful as a feed source for animals. Hence, *A. thaliana* does not have a "nutritional profile" as specified in the present claims, and there is no evidence that the modified *A. thaliana* plants obtained by Murata had an altered nutritional profile as presently claimed.

Murata also transformed rice, a water-intensive crop that is poorly adapted to dry climates, and which is not a crucifer. The accumulation of anti-nutritional phenolic compounds is therefore not of concern in rice. There is no evidence that the genetically altered rice plants of Murata had an altered nutritional profile as presently claimed. Applicants emphasize that Murata was concerned only with obtaining salt- or drought-tolerant plants useful for greening desert or salt-accumulated areas. Murata did not recognize or address the problem of reducing anti-nutritional compounds in plants, as in the instant invention.

New independent method claim 34, and the claims depending therefrom, include the steps of: (1) selecting a nucleic acid sequence for its ability to encode a protein capable of modifying the utilization of a sustrate in a secondary metabolic pathway associated with a nutritional profile of a plant; (2) transforming a plant cell of said

plant with an expression cassette comprising said nucleic acid sequence; and (3) recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant.

New independent claim 40 is similar, and specifies in the first step that the nucleic acid sequence is selected for its ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway.

Applicants respectfully submit that Murata, who was concerned only with producing a salt-tolerant plant, and was not concerned with the nutritional quality of the plant, does not teach or suggest this selection step, as presently claimed.

Further, there is no teaching or suggestion in Murata that the salt- or osmo-tolerant *A. thaliana* or rice plants obtained had an altered nutritional profile, as specified in the recovery step in instant claims 34 and 40.

New claims 49-65 are directed to a genetically modified cruciferous plant or a descendant thereof comprising: a recombinant nucleic acid sequence stably incorporated into the genome of said plant, said recombinant nucleic acid sequence encoding a protein which modifies the utilization of a substrate in the phenylpropanoid metabolic pathway of said plant, said plant having an improved nutritional profile relative to a wild-type of said plant. New claim 66, directed to an animal feed, also depends from claim 49.

As above, Applicants respectfully submit that Murata does not teach or suggest that a genetically modified plant having an improved nutritional profile relative to a wild-type plant, as instantly claimed.

For the foregoing reasons, Applicants respectfully submit that the instant claims are novel and inventive over Murata.

Claims 1-6 and 27-33 of record stand rejected under 35 USC § 102(b) as being anticipated by Van Ooijen *et al.* (U.S. Patent No. 5,543,576). The Examiner states that Van Ooijen *et al.* teach a method of making a genetically transformed plant comprising:

(a) introducing into a plant cell capable of being transformed and regenerated into a whole plant a DNA expression cassette comprising, in addition to DNA sequences required for transformation and selection in

plant cells, a DNA sequence that, under the control of a promoter active in plant cells, encodes phytase which a heterologous enzyme capable of modifying the utilization of the substrate anti-nutritional factor phytate, and

(b) recovering a plant which has an altered content of at least one product of the secondary metabolic pathway.

Applicants respectfully submit that the claims, as presently amended, patentably distinguish from Van Ooijen *et al.*

Independent method claim 34, and the claims depending therefrom, specify the step of "selecting a nucleic acid sequence for its ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant".

Van Ooijen *et al.* teach a method for catalyzing an enzyme-catalyzed reaction by adding to a reaction mixture seeds of a transgenic plant, which have been modified to contain an expression system for the production of a heterologous enzyme, specifically phytase. This method has the advantage of obviating the need for extracting and purifying the enzyme before using the enzyme to catalyze a reaction.

The instant specification addresses technology such as that described by Van Ooijen *et al.* at pages 27-30. At page 28, line 21, through page 29, line 3, the instant application explains that the transformation of plants with a heterologous phytase enzyme results in the liberation of phosphorus from phytic acid, but does not reduce the presence of complexed phytic acid or phytate (i.e. anti-nutritional compounds). That is, attacking the end product (i.e. phytic acid) with a phytase enzyme does not provide a solution to the problem of excess phytic acid.

In contrast, the present invention solves the problem by modifying the utilization of a substrate in a secondary metabolic pathway, rather than the end product, as taught by Van Ooijen *et al.* In a preferred embodiment of the present invention concerning phytic acid biosynthesis, the plant is transformed with a heterologous methyl transferase gene to specifically methylate myo-inositol, thereby modifying myo-inositol, so that it cannot be used as a substrate in phytic acid biosynthesis.

Hence, Van Ooijen *et al.* teach transformation of a plant with an enzyme that attacks the end product of a secondary metabolic pathway (i.e. phytic acid), rather than

transformation of a plant cell with a nucleic acid sequence selected for its ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, as claimed in instant claim 34. Therefore, Applicants respectfully submit that Van Ooijen *et al.* do not teach or suggest the method of instant claim 34.

Independent method claim 40, and the claims depending therefrom, specify the step of "selecting a nucleic acid sequence for its ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway of said plant."

Independent composition of matter claim 49, and the claims depending therefrom, specify "A genetically modified cruciferous plant or a descendant thereof comprising: a recombinant nucleic acid sequence stably incorporated into the genome of said plant, said recombinant nucleic acid sequence encoding a protein which modifies the utilization of a substrate in the phenylpropanoid metabolic pathway of said plant, said plant having an improved nutritional profile relative to a wild-type of said plant."

As discussed in the instant specification at e.g. the paragraph bridging pages 17 and 18, phytic acid is the end product in the sugar alcohol secondary metabolic pathway, not the phenylpropanoid metabolic pathway as claimed in instant claims 40 and 49. Van Ooijen *et al.* do not teach or suggest modifying the utilization of a substrate in the phenylpropanoid pathway as claimed in instant claims 40 and 49 and the claims depending therefrom.

Reconsideration and withdrawal of the rejections of the claims under 35 USC § 102 are therefore respectfully requested.

Concerning 35 USC § 103

Claims 3, 4, 15, and 33 of record stand rejected under 35 USC § 103(a) as being unpatentable over Murata in view of Willmitzer *et al.* (WO 92/01042).

Murata is discussed above herein. The Examiner acknowledges that Murata does not teach methods in which the promoter is tissue selective, or specifically seed selective (Office Action, page 5, first complete paragraph).

The Examiner contends that Willmitzer *et al.* teach transgenic plants expressing industrial enzymes, and methods for the production of such plants, and further that Willmitzer *et al.* teach that the DNA sequence encoding the enzyme of interest under the control of a promoter such as a seed specific promoter, such as the phaseolin

promoter. The Examiner further contends that Willmitzer *et al.* teach a variety of plants useful for the introduction of the enzyme, including tobacco, potato, tomato, pea, soy, and cereals, and further that either the entire plant or parts thereof maybe useful for animal feed.

The Examiner contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used seeds specific promoters for the expression of choline oxidase in plants as taught by Willmitzer *et al.* The Examiner contends that the ordinary practitioner would have been motivated to do so by the fact that choline oxidase is an enzyme which is sold commercially, and because Willmitzer *et al.* expressly teach that the production of enzymes in plants overcomes two major obstacles in enzyme production, the first being that higher plants have biosynthetic capacity to perform the requisite post-translational modifications occurring in eukaryotic cells of mammalian or other origin and secondly that transgenic plants grown in a field need little extra energy for growth and do not give rise to waste-management problems. The Examiner contends that Murata provides the nucleic acid sequence encoding choline oxidase and demonstrates that it can be successfully expressed in transgenic plants, and that Willmitzer *et al.* provide the necessary suggestion and direction to motivate the production of choline oxidase as is in plants, and thus, in the absence of secondary consideration such as unexpected results, the claimed invention is obvious over the prior art.

Applicants respectfully traverse this rejection.

It is accepted law that, to establish a *prima facie* case of obviousness, the first criteria that must be met is that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a reference or to combine the teachings of the references. See *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991).

Applicants respectfully submit that there is no motivation or suggestion to modify the process of Murata by using a tissue selective promoter, as taught by Willmitzer *et al.* In fact, such a combination would be unworkable. The primary reference, Murata, is directed to making transgenic plants that are salt-tolerant or osmo-tolerant. As discussed by Murata (see page 2 of the reference) salt-tolerant or osmo-tolerant plants would be useful for preventing global warming by greening uncultivated soils such as

desert or salt-accumulated soil. Murata was concerned with preparing plants that could grow under such conditions. Ideally, the entire plant would be salt-tolerant or osmo-tolerant. Murata teaches the expression of a heterologous choline oxidase gene in *Arabidopsis thaliana* or rice plants, so that glycinebetaine, an osmo-protective agent, accumulates in the plant. It would serve no purpose, and would indeed be contrary to Murata's purpose, if the choline oxidase gene were to be under the control of a tissue-selective promoter, such that glycinebetaine accumulated only in certain cells, so that the entire plant was not salt-tolerant or osmo-tolerant. Hence, modifying the teachings of Murata by using the tissue-specific promoter of Willmitzer *et al.* would go against Murata's intended purpose.

Applicants respectfully submit that, in order to establish a *prima facie* case of obviousness on the basis of modifying the teaching of one reference by the teaching of another reference, the proposed modification cannot render the prior art unsatisfactory for its intended purpose. If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. See *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Applicants respectfully submit that modification of the teachings of Murata by the teaching of Willmitzer *et al.* would render Murata unsatisfactory for its intended purpose, as discussed above, such that there is no suggestion or motivation to combine the references.

Instant claims 36-38 and 51-53 specify a tissue-selective promoter. For the above reasons, Applicants respectfully submit that a *prima facie* case of obviousness has not been established with respect to these claims. Reconsideration and withdrawal of the rejection of the claims under 35 USC § 103(a) are therefore respectfully requested.

Concerning Allowable Subject Matter

Applicants acknowledge the Examiner's finding that the subject matter of claim 10 of record is allowable, and that the prior art does not teach or suggest methods in which both choline oxidase and betaine aldehyde dehydrogenase are introduced into the same plant under the control of a seed-specific promoter. The subject matter of claim 10 is now found in claims 43, and 57.

In view of all the foregoing, entry of the amendments, reconsideration and withdrawal of the rejections of the claims, and timely issuance of a Notice of Allowance are respectfully requested.

Respectfully submitted,

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